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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Kazumori Funatsu

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YOUNG & THOMPSON
209 Madison Street
Suite 500
ALEXANDRIA, VA 22314

EXAMINER

NAFF, DAVID M

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/525,707	Applicant(s) FUNATSU ET AL.	
	Examiner David M. Naff	Art Unit 1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 December 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14, 17 and 30-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14, 17 and 30-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

An amendment of 12/29/08 amended claims 11-14 and 17, canceled claims 15 and 16, and added new claims 30-32.

Claims examined on the merits are 1-14, 17 and 30-32, which are all claims in the
5 application.

Claim Objections

Claim 1 is objected to because of the following informalities: in line 8, "provide" should be --- provided ---. Appropriate correction is required.

10 *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

15 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20 Claims 1-14, 17 and 30-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

25 Support is not found in the specification for "cells accumulated to form two or more layers in any radial direction" in lines 9-11 of claim 1. Paragraph 0091 of the published specification discloses "cells are accumulated to form two or more layers even though the cell aggregate (organoid) is cut any radical direction". It is unclear this means "cells accumulated to form two or more layers in any radial direction".

In the last two lines of claim 3, “flat form such that the form has a contact angle of 70 degrees or less” does not have clear support in the specification. Paragraph 0075 discloses “synthetic polymer having a contact angle of 70 degrees or less”. This does not disclose a “flat form” having the contact angle.

5 In the lines 9-14 of claim 17, “hollow portions of the hollow fiber membranes of the cell-filled device provide a communication path from the inlet to the outlet for the liquid to be treated” does not have clear support in the specification. Original claim 17 discloses a container having an inlet and outlet and “hollow fiber membrane type is separated from an external of the hollow forming a communication path of the liquid to be treated”. This does not set forth that the
10 communication is from inlet to outlet of the container.

The Markush group of shapes in claim 30 is not found in the specification. The shapes in paragraph 0070 are not the shapes of the Markush group.

The specification fails to disclose “triangle shape has concave sides” (claim 31) and “rectangle shape has concave sides” (claim 32).

15 ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20 Claims 1-14, 17 and 30-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, lines 5-7, “having inner walls which define hollow portions and modified cross-sections which are shaped as deformed perfect circles” is uncertain as to meaning and scope
25 and as to shapes that are deformed perfect circles. Does “deformed perfect circles” mean that a

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perfect circle hollow fiber has been modified in a process to provide a different cross-section shape, or that the hollow fiber cross-section is different from that of a perfect circle?

In lines 9-10 of claim 1, "cells accumulated to form two or more layers in any radical direction" is confusing and uncertain as to meaning since it is not seen how the procedure for filling the fibers described in the specification can result in layers. The amendment asserts that layers are formed because cells are filled in the hollow fiber at high density. However, filling at cell high density would not appear to produce cell layers.

Claims 3 and 6 are unclear as to the meaning and scope of "contact angle of 70 degrees or less", and how the contact angle defines the hollow fiber. The difference is a fiber having and not having the contact angle is uncertain. The amendment refers to paragraph 0075 of how to measure contact angle. However, the procedure described is very general and does not make clear the difference in the hollow fiber when having the contact angle and not having the contact angle.

Claim 3 is unclear as to cross-section that is flat form. The specification fails to define such a fiber in sufficient detail to enable one to know when a fiber cross-section is flat and not flat. The amendment refers to the upper right figure of Figure 3 as showing a flat fiber. However, it would be uncertain as to how much the cross-section can vary from that shown in the upper right figure and still be flat. The claimed flat cross-section does not have to have dimensions as shown by the upper right figure.

In claim 30, a shape that is a "diamond" is uncertain since diamonds can have many different shapes.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10

15

Claims 1-14, 17 and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Funatsu et al (6,284,451) in view of Gorsuch et al (6,802,820) (newly applied).

20

The claims require a cell-filled device comprising a hollow fiber membrane having inner walls which define hollow portions and modified cross-sections which are shaped as deformed perfect circles, and containing a cell aggregate in each of the hollow portions formed into two or more layers in any radial direction, and a distance from any point of the cell aggregate to the inner fiber wall cannot be 75 μ m or more. Also claimed is a hybrid artificial organ containing the device.

25

Funatsu et al disclose using centrifugal force to fill a hollow fiber membrane with cells such as hepatocytes, and culturing the cells in the hollow fiber to form a cell aggregate. For example, see col 4, line 50 to col 11, line 4. The hollow fiber containing the cell aggregate can be used to form a hybrid artificial organ (col 2, line 47).

Gorsuch et al disclose hollow fiber membranes for *in vivo* plasmapheresis and ultrafiltration. The hollow fiber membrane is tubular in shape and generally circular in cross-section (col 2, lines 13-15).

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It would have been obvious to use in Funatsu et al a hollow fiber that is generally circular in cross-section as disclosed by Gorsuch et al since the inner diameter of the hollow fiber of Funatsu et al can vary (col 5, lines 15-20 and paragraph bridging cols 6 and 7), and a hollow fiber having a generally circular cross-section would have been expected to provide the results disclosed by Funatsu et al. A cross-section that is generally circular is not a perfect circle, and can be considered as a modified cross-section shaped as a deformed perfect circle. There is no requirement in Funatsu et al to use hollow fiber having a cross-section that is a prefect circle. The hollow fiber containing a cell aggregate disclosed by Funatsu et al is a cell-filled device. Cells contained by the cell aggregate in the hollow fiber of Funatsu et al are inherently in the form of two or more layers in any radial direction. A distance of not more than 75 μm or more from any point of the cell aggregate to the inner wall of the hollow fiber is inherent when certain dimensions of the cross-section of the hollow fiber are selected. The membrane fiber of Funatsu et al inherently has a pore size as required by claims 4 and 5, a polymer contact angle of claim 6, polymers as required by claims 7-9, cells as required by claims 10-13 and sealed ends as required by claim 14. The hollow fiber containing a cell aggregate of Funatsu et al can be used to form a hybrid artificial organ. When using a fiber that is not a perfect circle to contain the cell aggregate as set forth above, it would have been obvious to form a hybrid artificial organ containing the fiber. Selecting a shape as in claims 30-32 would have been merely a matter of individual preference. The shapes of the claims have not been established to provide a result different than when using a hollow fiber having a generally circular cross-section as suggested by Gorsuch et al. A flat cross-section as in claim 3 would have been a matter of obvious choice depending on individual preference, and would have been expected to provide the same function as a generally circular cross-section. A flat cross-section has not been established to provide a new and unexpected result.

Response to Arguments

The amendment urges that Funatsu et al use a conventional hollow fiber with an unmodified cross-section, i.e. the shape is a perfect circle. However, Funatsu et al nowhere disclose that the hollow fiber must be a perfect circle, and do not disclose using a hollow fiber
5 having the cross-section of a perfect circle. Most hollow fibers will have a cross-section that is slightly different from a perfect circle due to lack of sufficient control in the manufacturing process to produce a cross-section that is a perfect circle. In any event, when Gorsuch et al is considered, it would have been obvious that the cross-section can be generally circular and does not have to be a perfect circle. A hollow fiber that is not a perfect circle inherently has a
10 modified cross-section shaped as a deformed perfect circle. The claims do not require beginning with a hollow fiber having a cross-section of a perfect circle and modifying the perfect circle cross-section by pressing the hollow fiber between plates as in Figure 2 (1) or by pressing hollow fiber between rollers as in Figure 2 (2). The claims encompass a hollow fiber that is produced initially not having a perfect circle cross-section. Funatsu et al disclosing a
15 hollow fiber diameter of 285 μm does not necessitate that the hollow fiber be perfect circle.

The amendment urges that using a hollow fiber cross-section that is not a perfect circle results in a smaller distance to cells so that necrosis is prevented as shown by Figure 6 as well as other problems involved with using a perfect circle cross-section. However, the hollow fiber in Figure 6 that results in no necrotized layer is the right figure that is in the form of a flat cross-
20 section having specific dimensions, which are not required by the present claims. Middle figure in Figure 6 is not a perfect circle and appears to contain a necrotized layer about the same as the left perfect circle control. The present claims do not require the cross-section dimensions of the right Figure 6, and the claims encompass a hollow fiber cross-section only slightly different from the dimensions of a perfect circle which would result in a necrotized layer not substantially

different from using a perfect circle. A perfect circle cross-section and cross-sections slightly different can provide a distance of not over 75 μm to any point of a cell aggregate in the hollow fiber if the perfect circle cross-section of the hollow fiber is sufficiently small. The amendment urges that not using perfect circle cross-section enables using a cross-section volume greater
5 than a perfect circle and not obtaining a necrotized layer. However, the claims do not require the non-perfect circle cross-section to have dimensions that would provide a greater volume in the hollow fiber without producing a necrotized layer than a fiber having a perfect circle cross-section that results in a necrotized layer.

Conclusion

10 Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the
15 mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20 Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent

5 Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you
10 would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David M. Naff/
Primary Examiner, Art Unit 1657

15 DMN
4/28/09